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BACKGROUND

Long-term antipsychotic drug usage is the cornerstone of schizophrenia treatment. Antipsychotic drugs not only control symptoms by affecting dopaminergic neurotransmission, but also cause side effects including hyperprolactinemia. Prolactin secretion is persistently inhibited by dopamine, and antipsychotic drugs are believed to increase prolactin release by blocking dopamine receptors in the pituitary gland.

Genes coding for dopamine receptors and transporters are considered as candidate genes responsible for the antipsychotic-induced hyperprolactinemia (HP).

OBJECTIVE

The present study aimed to investigate the role of polymorphisms of the dopamine receptors and transporters genes (*DRD1, DRD2, SLC6A3*) in the pathogenesis of antipsychotic-induced HP in patients with schizophrenia.

METHODS

- 431 Russian patients with schizophrenia were examined. The average age of these patients was 42.1±1.4 years.
- Serum prolactin (PRL) levels were measured using AccuBind ELISA Microwells kit (Monobind Inc., USA)). The upper limits for normal PRL concentration were set at ≤20 ng/ml for men and ≤25 ng/ml for non-pregnant, non-nursing women.
- Genotyping was carried out of 17 polymorphic variants of the dopamine receptors genes *DRD1, DRD2* and dopamine transporter gene *SLC6A3*, with the use of MassARRAY® Analyzer 4 (Agena Bioscience™).
- SPSS software was used for statistical analysis. The Hardy-Weinberg equilibrium (HWE) of genotypic frequencies was tested by the chi-square test.

RESULTS

All patients with schizophrenia were divided into two groups: those with and without HP. Patients from both groups were genotyped for *DRD1* variants: *rs4532, rs936461;* for *DRD2* variants*: rs4245147, rs6279, rs2734842* and for *SLC6A3* variants*: rs3756450, rs2550956, rs6347, rs2617605, rs3863145, rs250686, rs464049, rs4975646, rs1048953, rs11133767, rs27048, rs40184.*

Statistically significant result was obtained for polymorphic variant *rs2550956* of the gene *SLC6A3* (χ^2 = 9,992; p = 0,007), which suggests its involvement in the development of HP. The heterozygous genotype *TC* of *rs2550956* was significantly less common in patients with elevated levels of prolactin and it presumably has protective properties (OR 0,54; 95% CI: 0,36 – 0,81).

Table 1 – Distribution of genotypes and alleles of polymorphic variant *rs2550956* of the gene *SLC6A3* between patients with and without hyperprolactinemia (HP)

Gene	Geno types	Patients with HP	Patients without HP	χ^2	p
SLC6A3 *rs2550956*	TT TC CC	113 (49,8%) 89 (39,2%) 25 (11,0%)	123 (56,9%) 56 (25,9%) 37 (17,1%)	9,992	**0,007**
	T C	315 (69,4%) 139 (30,6%)	302 (69,9%) 130 (30,1%)	0,030	0,870

CONCLUSION

Our results indicate that genetic variants of *SLC6A3* is associated with functional consequences on the modulation of prolactin secretion. Neurotransmitter systems are involved in the mechanisms of action of antipsychotic drugs; therefore, a further search for genetic markers associated with the development of side effects of antipsychotic therapy is needed, that will contribute to the development of effective methods of diagnosis, correction and treatment of schizophrenia, as well as of compliance of patients with mental disorders to psychotropic therapy.